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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,493	07/07/2005	Valerie Autier	MERCK-3029	1128

23599 7590 09/20/2007

MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER	
HUGHES, ALICIA R	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
09/20/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,493	AUTIER ET AL.	
	Examiner	Art Unit	
	Alicia R. Hughes	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11-29,33,55 and 56* is/are pending in the application.

4a) Of the above claim(s) *2-5,9,11-13,16-18,22,28 and 29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-8,14,15,19-21,23-27,33,55 and 56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *07 July 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2 sheets*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1, 6-8, 14, 15, 19-21, 23-27, 33, 55 and 56 are pending and the subject of this Office Action. Applicant cancelled claims 10, 30-32, and 34-54 in the response filed on 25 January 2007.

Claims 2-5, 9, 11-13, 16-18, 22, 28 and 29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species and a non-elected invention, there being no allowable generic or linking claim.

Applicant's election of species, with traverse in the reply filed on 22 January 2007 and maintained on 13 July 2007, is acknowledged.

The traversal of the restriction requirement is deemed moot, as Applicant has cancelled all claims in Groups II and III presented previously for examination.

With regard to the traversal of the specie election for a compound, for the purposes of examination herein, the search has been extended past the elected species, because prior art was not found.

Claim Rejections - 35 U.S.C. §112.1

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the

> best mode contemplated by the inventor of carrying out his invention.

Claim 33 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Claim 33 is drawn to certain compounds "or a pharmaceutically acceptable prodrug thereof" The specification is written broadly, simply advising that "'prodrugs' means compounds which, once administered to the patient, are chemically and/or biologically transformed by the living body into compounds of the formula (I) or (II) (Specification, page 20, lines 13-15), noting that "[e]xamples of prodrugs of the formula (I) above are those for which R4 represents a radical –OP, in which P is a leaving group, for example a sugar residue, such as sucrose, which can thus lead to compounds in which R^4 represents –OH." (Specification, page 20, lines 16-19). Such a single reference is insufficient to meet the written description proviso of 35 U.S.C. 112, first paragraph.

Claims 1, 6-8, 14, 15, 19-21, 23-27, 33, 55 and 56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 1 is enabled for the treatment of diabetes or associated complications by the administration of an effective amount of a compound that inhibits kynurenine 3-hydroxylase. However, the claimed prevention of the same, *supra*, is not supported by the specification. As a

result, the effect of performing the invention by one skilled in the art would be that of undue experimentation.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in organic chemistry is high, the results of experiments to discover treatments for the illnesses and conditions recited in claim 17, is unpredictable. While all of the Wands factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The applicant has provided a number of working examples for producing chemical compositions that treat diabetes and related complications. And further, Applicant has also referenced examples of chemical mixtures that will support the invention (Specification, pages 37-53). However, the applicant has failed to enable the prophylaxis, or prevention, of any of the above conditions noted in the claimed invention through the examples provided. Prophylaxis is generally defined as "the preventing of disease." Random House Unabridged Dictionary, Random House, Inc. 2006. Given the state of the art, namely the numerous divergent factors that may contribute to one acquiring diabetes it is unreasonable to believe a manner of prevention of

diabetes predictable even amongst similarly aged, for example, populations, even in light of the specification's disclosures.

As such, the art of the claimed invention lacks predictability because the claim as written to include prevention of diabetes and related complications.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned

with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 6-8, 14, 15, 19-21, 23-27, 33, 55 and 56 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-21, 27, 28 and 30-33 of U.S. Patent Application No. 10/541,377. Although the conflicting claims are not identical, they are not patentably distinct from each other, because they contain overlapping/closely related subject matter, most notably, the treatment of diabetes and related complications by administering to a patient in need thereof a kynurenine 3-hydroxylase inhibitor.

Claim Rejections – 35 U.S.C. §102(b)

The following is a quotation of 35 U.S.C. §102(b), which forms the basis for all obviousness rejections set forth in this Office Action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6-8, 33, and 55-56 are rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 6,323,240 B1 [hereinafter referred to as "Giordani et al"] as evidenced by U.S. Patent No. 6,572,542 [hereinafter referred to as "Houben et al"].

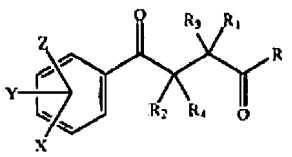
Giordani et al teach a class of 4-phenyl-4-oxobutanoic acid derivatives and their pharmaceutically acceptable salts (Abstract) with a core structure that encompasses the core structure of the present invention useful in the treatment of glaucoma/retinopathy (Col. 3, lines 4-

20). Giordani et al also teach that the 4-phenyl-4-oxobutanoic acid derivatives are used as a kynurenine-3-hydroxylase inhibitor (Col. 3, limes 4-5). It is well understood in the art that retinopathy is a known complication associated with diabetes (Houben et al, Col. 1, lines 38-67; *see also* Diabetes Research Foundation, "Diabetes and Your Eyesight," printed from http://www.glaucoma.org/learn/diabetes_and_yo.html, 2 pages), as reported in the Fall 1998, ed. of *Gleams*, an electronic publication of the Glaucoma Research Foundation.

More specifically, as with the present invention, Giordani et al disclose the following

Accordingly, the present invention provides a 4-phenyl-4-oxo-butanoic acid derivative of formula (I) either as a single isomer or as mixture of isomers

(I)



wherein

X, Y and Z are, each independently, hydrogen, halogen, cyano, nitro, C_1–C_6 alkyl, phenyl, benzyl, C_2–C_4 alkenyl, C_2–C_4 alkynyl, C_1–C_6 alkoxy or C_1–C_6 alkylthio;

R is hydroxy; —OR_5 in which R_5 is C_1–C_6 alkyl, phenyl, benzyl, C_2–C_4 alkenyl or C_2–C_4 alkynyl; —$N(R_6)_2$ or —$N(R_6)OR_6$ in which each R_6 is, independently, hydrogen, C_1–C_6 alkyl, C_2–C_4 alkenyl, C_2–C_4 alkynyl, phenyl or benzyl;

R_1, R_2, R_3 and R_4 are, each independently, hydrogen, halogen, hydroxy, thiol, C_1–C_6 alkoxy, C_1–C_6 alkylthio, C_1–C_6 alkyl, C_2–C_4 alkenyl, phenyl or benzyl, or

R_1 and R_3 or R_2 and R_4 together form a group =CHR_8 in which R_8 is hydrogen, a straight C_1–C_5 alkyl chain or phenyl;

(Col. 2, lines 38-67).

In the present invention, R^1 may represent a heterocyclic radical, which could be identical to the phenyl ring disclosed in Goirdani et al. The present invention's R^2 is the equivalent of Giordani's R^2, and the present invention's R^3 is the equivalent of Girodani's R^4. According to Giordani, both its R^2 and R^4, just as its R^3 and R^1, can be hydrogen, halogen, thiol, alkenyl,

alkoxy, etc., just as the present invention's R^2 and R^3 positions can be the same. The present invention's W represents a divalent radical which is the equivalent to the cycloalkyl formed in Giordani et al that includes R^1 and R^3, and finally, R^4 in the present invention, which is the equivalent of R in Giordani et al, can both be, for example, a heterocyclic ring or an alkenyl or alkyl.

In light of the foregoing, a method of treating diabetes and associated complications by the administration of a 4-phenyl-4-oxobutanoic acid derivatives used as a kynurenine-3-hydroxylase inhibitor, is clearly anticipated.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alicia Hughes whose telephone number is 571-272-6026. The examiner can normally be reached from 9:00 AM to 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached at 571-272-0718. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR of Public PAIR. Status information for unpublished applications is available through Public PAIR only. For information about the PAIR system, see http://pair-direct-uspto.gov. Should you have questions on access to the Private PAIR system,

contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

16 April 2007
ARH

9/16/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER